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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)

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on _____

Signature Shih-Chieh Hung

Typed or printed name Shih-Chieh Hung

Application Number	Filed
09/761,893	01/17/2001

First Named Inventor: Shih-Chieh Hung

Art Unit	Examiner
1636	Jennifer Dunston

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [x] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [ ] attorney or agent of record. Registration number _____
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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February 3, 2012
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Shih-Chieh Hung	ART UNIT: 1636
APPLICATION No.: 09/761,893	EXAMINER: Jennifer Dunston
FILING DATE: 01/17/2001	

FOR: Method of isolating mesenchymal stem cells

PRE-APPEAL BRIEF REQUEST FOR REVIEW

In response to the Final Office Action mailed on November 17, 2011 and Advisory Action mailed on January 11, 2012, finally rejecting claims 1, 4, 6, 9-11, 34-35 and 38, applicants hereby request Panel Review. The rejections of record are not proper and are without basis, as set forth below. Claims 1, 4, 6, 9-11, 34-35, 38 and 43-45 are pending.

REMARKS

Claims 1, 4, 6, 9-11, 34-35 and 38 have been rejected under 35 U.S.C. §103(a) in the Office Action dated on November 17, 2011 and January 11, 2012. Claims 43-45 have been pending since June 14, 2011 but were without consideration by the Examiner.

Overview

Applicants' invention related to a method for isolating mesenchymal stem cells (MSCs) from bone marrow aspirate. The instant invention is based on the discovery that the recovering efficiency of MSCs is significantly improved by the combination of isolating and culturing MSCs. Applicants were the first to recognize the method for recovering MSCs by means of combining the MSCs' physical characteristics and biological properties.

As described in the specification, "in one preferred embodiment, cell populations having greater than 98% of human MSCs can be obtained in accordance with the method of the invention, and such isolated MSCs can proliferate without differentiation and reach confluence even after 12 passages." [0011] Applicants also demonstrated that "the late adhering cells maintained homogeneous morphology (referring to FIG. 1(a)) and were significantly greater in number than the same cells cultured by the conventional methods." [0039]

Rejection Under 35 U.S.C.§103(a)

The Office Actions fails to provide a proper basis for support obviousness rejection. The Office Actions repeatedly rejected the Claims 1, 4, 6, 9, 11, 34, 35 and 38 under 35 U.S.C. 103(a) over Caplan et al (US patent 5811094) in view of Prockop et al (US patent 7374937) and Matsui et al (US patent 4871674). However, the Office Action only stated "it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of isolating MSCs of Caplan et al to include the introduction of the mixed composition of cells comprising MSCs and medium into the culture dish taught by Matsui et al because Caplan et al teach that MSCs adhere to plastic for culturing, and Caplan et al teach it within the ordinary skill in the art to use a filter to remove fat cells and red blood cells from cells of bone marrow. Furthermore, Prockop et al teach the collection of MSCs on a filter of polycarbonate containing 10 micrometer pores; Matsui et al teach culture cells in a device comprising a polycarbonate filter. One would have been motivated to make such a modification in order to receive the expected benefit of providing an enriched population of MSCs without having to perform the extra steps of using a separate filter, or other separation method, as taught by Caplan et al, since red blood cell removal and MSCs culture could be performed simultaneously using the culture dish of Matsui et al. Based upon the teachings of cited references, the high skill of one of

ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention" (Office Action mailed on November 17, 2012, p6)

No prior art would have suggested to those of ordinary skill in the art that they should carry out the claimed method as this Application. Moreover, no prior art would have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. The disclosure of the applicant cannot be used to hunt through the prior art for the claimed elements and then combine them as claimed. In re Laskowski (Fec. Cir. 1989). Furthermore, "to imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teachers" W.L. Gore & Associates, Inc. v. Garlock Inc. (Fec. Cir. 1983).

On the contrary, Matsui et al's disclosure (US patent 4871674) was criticized to be "In the use of these cell culture inserts, gases may not be exchanged sufficiently because the area between the sidewall of the insert and the culture plate is too small." (Column 1, line 37 to 39 US patent 5652142). Thus, one of the ordinary skills in the art would run into difficulty to adopt Matsui's device as the upper plate of this application. Furthermore, The Matsui's 4871674 patent was issued on 10/3/1989. Caplan's 5811094 patent was applied on 4/11/1995 and issued on 9/22/1998. Prockop's 7374937 patent was applied on 10/25/2000 (effective date 3/14/2000). This application was filed on 1/17/2001 with the priority date on 10/17/2000. The time frame highly did not support the Office Action that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine these three prior arts and do some modifications." If it had been obvious, Prockop would have combined the teachings of Matsui and Caplan to reach the method recited in this application. Moreover, Prof. Prockop has been a well known mesenchymal stem cell researcher in the US and the world, but did not reach the method of this application. It would be one of strong evidences that "one of ordinary skill in the art could not have combined the claimed elements by known methods (e.g., due to technological difficulties)" MPEP 2141

Prockop et al's disclosure was quietly close to that of this Application, which would present the state of art in the year of 2000. The specification of Prockop et al (US patent 7374937) clearly disclosed that "However, prior art methods for isolating MSCs and inducing their proliferation have practical limitations, including the extent of population expansion that can be achieved using prior art methods. There remains a critical need for methods of reliably inducing significant proliferation of MSCs in culture without inducing differentiation of the MSCs as they proliferate." (Column 5, line 21 to line 28) Moreover, the post-filling art (Kato et al US Patent Application 20050013804, filling date: 09/12/2001) also presents the state of

art close to this Application, which mentioned that "The conventional culture methods however cannot produce sufficient amounts of mesenchymal stem cells because the proliferation of said stem cells stops or becomes extremely slow around 15th generation." No prior art would have suggested that one of ordinary skill in the art could modify Caplan's disclosure in the way of this Application. One of ordinary skill in the art would not have recognized that the results of the combination of Caplan, Matsui and Prockop were predictable. Indeed, no prior art would have revealed that the combination would improve the culture efficiency, as this Application disclosed.

The Claims 1, 4, 6, 9, 11, 34, 35 and 38 were rejected under 35 U.S.C. 103(a) over Caplan et al in view of Burkitt et al (Wheater's Functional Histology, 1993 page 60) and Matsui et al. (Office Action mailed on November 17, 2012, p8). Similarly, the Office Actions fails to provide a proper basis for support obviousness rejection. The Office Action only stated but not provided any prior art which would have suggested to those of ordinary skill in the art that they should carry out the claimed method as this Application. No prior art would have revealed that those of ordinary skill would have a reasonable expectation of success to carry out Caplan et al's disclosure in view of Burkitt et al and Matsui et al. Moreover, as discussed above, Matsui et al's disclosure was critized by others. Those of ordinary skill would not have used Matsui et al's teaching. Furthermore, Burkitt et al's and Matsui et al's teaching were many years before Caplan et al's as well as Prockop et al's applications. These two leading teams as well as others did not carry out the claimed method as this Application. Thus, the Office Actions fails to provide a proper basis for support obviousness rejection.

The Claims 1, 4, 6, 9, 11, 34, 35 and 38 were also rejected under 35 U.S.C. 103(a) over Caplan et al in view of Guirguis (US patent 5077012) and Matsui et al. (Office Action mailed on November 17, 2012, p12). Again, the Office Actions fails to provide a proper basis for support obviousness rejection. Guirguis did teach the membrane with 2 microns or less to filter red blood cells and protein. No suggestion would have suggested to those of ordinary skill in the art that they should modify Caplan et al's disclosure in view of Burkitt et al and Matsui et al as this Application claimed. Moreover, no prior art would have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success.

Pending claims without consideration by the Examiner

The amendments dated on June 14, 2011, July 19, 2011, September 15, 2011 and December 19, 211 listed pending claims 43, 44 and 45. However, the Office Actions dated on August 31, 2011, November 17, 2011 and January 11, 2012 repeated ignoring the pending request.

This application disclosed that "in one preferred embodiment of the present invention, the isolated mesenchymal stem cells proliferate without differentiation and

reach confluence even after 12 passages. The cell populations having greater than 98% homogeneous MSCs are obtained in accordance with the method of the present invention."[0031] This application adds theses "unexpected results" in claims 43-45. (MPEP 2145 & 716.02) The unexpected results was supported by post-filling art (Kato et al US Patent Application 20050013804, filling date: 09/12/2001), which mentioned that "The conventional culture methods however cannot produce sufficient amounts of mesenchymal stem cells because the proliferation of said stem cells stops or becomes extremely slow around 15th generation."

Conclusion

As set forth in 35 U.S.C.§103(a), "a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." However, a claim "composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, know in the prior art." KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 418 (2007).

As discussed above, the Office Actions fails to provide a proper basis for support obviousness rejection. Indeed, no prior art would have suggested to those of ordinary skill in the art that they should carry out the claimed method as this Application. Moreover, no prior art would have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Furthermore, the instant invention is based on the discovery that the recovering efficiency of MSCs is significantly improved by the combination of isolating and culturing MSCs. Applicants were the first to recognize the method for recovering MSCs by means of combining the MSCs' physical characteristics and biological properties. The specification did demonstrate the unexpected results.

A Notice of Allowance is respectfully requested.

Respectfully submitted:
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